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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/486,334	07/18/2000	MICHEL DROUX	PH-98/080	6869

7590 04/29/2003

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EXAMINER
KUBELIK, ANNE R

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 04/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/486,334	DROUX ET AL.	
	Examiner	Art Unit	
	Anne R. Kubelik	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 December 2002 and 22 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *2-7,9-11,13,15-26 and 31-73* is/are pending in the application.

4a) Of the above claim(s) *7,10,11,15,16,21,22 and 31-59* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *2-6,9,12,13,17-20,23-26 and 60-72* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 October 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 17 December 2002 has been entered.

2. The substitute specification, the amendment to the specification, the amendments to claims 5, 13, 20, 23 and 60, and the addition of claims 72-73, requested in Paper No. 19, filed 22 October 2002, have been entered. The amendments to claims 20 and 72 requested in Paper No. 26, filed 17 December 2002 have been entered.

Claims 7, 10-11, 15-16, 21-22 and 31-59 remain withdrawn from consideration, as being drawn to nonelected inventions. Applicant is reminded that complete reply to a final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144). See MPEP § 821.01.

Claims 2-6, 9, 13, 17-20, 23-26 and 60-73 are examined to the extent they read on SEQ ID NO:1, which encodes the *Arabidopsis* cytoplasmic SATase, SAT3.

3. The disclosure is objected to because it contains embedded hyperlinks and/or other forms of browser-executable code. See paragraph [0111]. Applicant is required to delete the embedded hyperlinks and/or other forms of browser-executable code. See MPEP § 608.01.

4. The disclosure is objected to because it lacks a Brief Description of each Figure.

5. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825.

Sequence identifiers are missing from either the legend or the Brief Description of Figures 4-9.

Full compliance with the sequence rules is required in response to this Office action. A complete response to this Office action must include both compliance with the sequence rules and a response to the issues set forth below. Failure to fully comply with both of these requirements in the time period set forth in this Office action will be held to be non-responsive.

6. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Response to Arguments

7. The rejection of claims 17, 19, 23, 25, 60 and 70-71 under 35 USC 112, is paragraph, for lack of deposit of a plasmid is withdrawn in light of Applicant's pointing out where the optimized transit peptide is taught in the specification.

Claim Objections

8. Claims 2-6, 9, 13, 17-20, 23-26, 61-71 and 73 are objected to because of the following informalities:

Claims 2-6, 9, 13, 17-20 and 23-26 lack an article at the start of the claim.

In claims 2-6, 9, 13, 17-20, 23-26, "characterized in that" should be replaced with --wherein--.

In claims 13 and 19, line 3, --wherein-- should be inserted after "protein," and "being" should be replaced with --is--.

In claim 13, line 4, an article is missing before "mitochondria".

In claim 18, line 3, --wherein the DNA sequence-- should be inserted after "acetyltransferase,".

In claim 19, line 4, an article is missing before "chloroplasts".

In claims 61-71 and 73, a comma should be inserted before "wherein".

Claim Rejections - 35 USC § 112

9. Claims 2-3, 5-6, 13, 17-20, 23-26, 60-61 and 63-72 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of increasing the production of cysteine, glutathione, methionine and sulfur derivatives in a plant by transformation with a gene encoding a cysteine-insensitive plant SATase, does not reasonably provide enablement for methods of increasing the production of cysteine, glutathione, methionine and sulfur derivatives in a plant by transformation with a nucleic acid encoding a cysteine-sensitive SATase or plant SATase rendered cysteine-insensitive by mutagenesis. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The rejection is modified from the rejection set forth in the Office action mailed 17 June 2002, as applied to claims 2-6, 9, 12-13, 17-20, 23-26 and 60-71. Applicant's arguments filed 22 October 2002 have been fully considered but they are not persuasive. Applicant filed no arguments in the response of 17 December 2002.

The claims are broadly drawn to a method for increasing the production of cysteine, glutathione, methionine and any sulfur derivative by overexpression of any SATase by transformation of the plant with a nucleic acid encoding the SATase.

The instant specification, however, only provides guidance for a method of assaying the inhibition of pea SATase isoforms by cysteine to show that the mitochondrial form is severely inhibited by cysteine, the cytoplasmic form is moderately inhibited and the cytosolic form is not inhibited at all (example 1); the specification states that in *Arabidopsis* the chloroplast enzyme is cysteine-insensitive and that which form is insensitive and which sensitive is plant dependent (example 1); analysis of the mode of inhibition by cysteine to show that it a non-competitive inhibitor (example 1); isolation of the cytoplasmic SATase (SAT3, SEQ ID NO:1, which encodes SEQ ID NO:2) from *Arabidopsis* by functional complementation of an *E. coli* mutant (example 2); overexpression of SAT3 in *E. coli* and isolation of the protein to show it is cysteine-insensitive (example 3); isolation of other SATases from *Arabidopsis*, including SAT3'(SEQ ID NO:3), another cytosolic form (example 4), SAT1' (SEQ ID NO:5), a cytosolic form (examples 5 and 11), SAT1 (SEQ ID NO:7), a mitochondrial form (example 5), SAT2 (SEQ ID NO:9) a chloroplastic form (example 7), and SAT4 (SEQ ID NO:11), another chloroplastic form (example 8); overexpression of SAT1 in *E. coli* and isolation of the protein to show it is cysteine-insensitive (example 6). The specification provides guidance for the transformation of tobacco with a nucleic acid encoding one of these SATases with and without the OTP (examples 9-10), that plants transformed with a nucleic acid encoding cysteine-insensitive SAT3, SAT1' or SAT1 have increased levels of cysteine, glutathione and methionine, compared to untransformed plants (examples 11-13).

The specification fails to provide guidance for methods of increasing the production of cysteine, glutathione, methionine and any sulfur derivative by overexpression of a cysteine-sensitive SATase. The specification in paragraph [0021] states that cysteine induced inhibition of SATase is a limiting factor in the synthesis of cysteine. A cysteine-sensitive SATase would

be inhibited in the transformed plants, and these plants would not have higher levels of cysteine, glutathione, methionine or methionine-derivatives. Applicant is invited to submit a declaration presenting data showing that plants transformed with a nucleic acid encoding a cysteine-sensitive SATase have higher levels of cysteine, glutathione, methionine or methionine-derivatives than non-transformed plants.

Claim 5 is drawn to a method of overexpressing a plant SATase rendered cysteine-insensitive by mutagenesis. The instant specification, however, fails to provide guidance for which amino acids of the SATase to alter and to which other amino acids, and which amino acids must not be changed, to maintain SATase activity and to convert a cysteine-sensitive SATase to a cysteine-insensitive one.

Making substitutions in proteins does not produce predictable results. Lazar et al (1988, Mol. Cell. Biol. 8:1247-1252) showed that the "conservative" substitution (*e.g.*, substituting one polar amino acid for another, or one acidic one for another) of glutamic acid for aspartic acid at position 47 reduced biological function of transforming growth factor alpha while "nonconservative" substitutions with alanine or asparagine had no effect (abstract). Similarly, Hill et al (1998, Biochem. Biophys. Res. Comm. 244:573-577) teach that when three histidines that are maintained in ADP-glucose pyrophosphorylase across several species are substituted with the "nonconservative" amino acid glutamine, there is little effect on enzyme activity, while the substitution of one of those histidines with the "conservative" amino acid arginine drastically reduced enzyme activity (see Table 1). Thus, making substitutions in proteins to alter activity is unpredictable.

Given the claim breath, unpredictability, and lack of guidance as discussed above, undue experimentation would have been required by one skilled in the art to convert a nucleic acid

encoding a cysteine-sensitive SATase to a cysteine-insensitive one. Making all possible single amino acid substitutions in a 300 amino acid long protein like a typical SATases would require making and analyzing 19^{300} nucleic acids.

As the specification does not describe the transformation of any plant with a nucleic acid encoding an SATase that had been converted from a cysteine-sensitive SATase to a cysteine-insensitive one, undue trial and error experimentation would be required to screen through the myriad of nucleic acids encompassed by the claims and plants transformed therewith, to identify those with increased levels of cysteine, glutathione, methionine or sulfur-containing derivatives of methionine, if such plants are even obtainable.

Given the claim breath, unpredictability in the art, undue experimentation, and lack of guidance in the specification as discussed above, the instant invention is not enabled throughout the full scope of the claims.

Applicant urges that the specification teaches cysteine-sensitive and -insensitive forms of SATase. Applicant urges that example 13 plants transformed with a nucleic acid encoding a cysteine-sensitive SATase had an increase in cysteine, methionine and glutathione; thus the examples overcome unpredictability (response pg 5-6).

This is not found persuasive because Example 13 teaches plants transformed with SAT1, which example 6 teaches is cysteine-insensitive. Thus, unpredictability has not been overcome by the examples.

Applicant urges that SATases rendered cysteine-insensitive by mutagenesis are referred to at pg 9, lines 22-27, of the specification; the references cited therein show which part of the sequences can be modified (response pg 6-7).

This is not found persuasive. Two references were cited in that section of the specification (paragraph 0027 in the substitute specification), Nakamori et al and Takagi et al; Nakamori et al was cited in the IDS of Paper No. 6, while Takagi et al could not be considered because it was not sent. The mutations taught in Nakamori et al are to a methionine at position 256; the Arabidopsis enzymes do not have a methionine at this position, and the specification provides no teachings of what would be equivalent of Met_{256} in Arabidopsis.

Applicant urges that optimized transit peptide is taught in US Patents RE36,449 and RE 37,287, sent with the response. Applicant also urges that Turk et al is directed to vacuolar targeting, not mitochondrial or chloroplast targeting (response pg 7-8).

This portion is the rejection is withdrawn.

Applicant urges that SATases from plants other than Arabidopsis are well known in the art and cited in the specification (response pg 8-9),

This portion is the rejection is withdrawn.

10. Claims 4-5 and 60 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is modified from the rejection set forth in the Office action mailed 17 June 2002, as applied to claims 2-6, 12-13, 17-20, 23-26 and 60-71. Applicant's arguments filed 22 October 2002 have been fully considered but they are not persuasive. Applicant filed no arguments in the response of 17 December 2002.

The claims are broadly drawn to method of using a nucleic acid encoding an SATase that had been converted from a cysteine-sensitive SATase to a cysteine-insensitive one. The specification, however, does not teach such a nucleic acid.

Hence, Applicant has not, in fact, described nucleic acid encoding an SATase that had been converted from a cysteine-sensitive SATase to a cysteine-insensitive one. Because the sequences are not described, the method of using the sequences to increase the production of cysteine, glutathione, methionine or sulfur-containing derivatives of methionine in a plant or plant cell is likewise not described, and the specification fails to provide an adequate written description of the claimed invention.

Therefore, given the lack of written description in the specification with regard to the structural and physical characteristics of the compositions used in the claimed methods, it is not clear that Applicant was in possession of the genus claimed at the time this application was filed.

Applicant urges that *Vas Cath* states that words, structures, figures, diagrams, and formulas may be used to show an Applicant was in possession of the invention. Applicant urges that pg 9, lines 22-27 of the specification, and the references cited therein, refer to SATases rendered cysteine-insensitive by mutagenesis (response pg 10-).

This is not found persuasive because the cited references, in so far as they were sent, do not describe plant SATases rendered cysteine insensitive.

11. Claims 2-6, 9, 13, 17-20, 23-26 and 60-73 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention. Dependent claims are included in all rejections. The following rejections are new. The previous rejections are withdrawn, due to amendment.

The term "increasing" in claims 60 and 72 is a relative term that renders the claim indefinite. The term "increasing" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be

reasonably apprised of the metes and bounds of the invention. There is no reference for comparison for the increase; it is suggested that the levels be compared to the levels in a nontransformed plant.

In claim 60, the placement of the phrase "or in plants containing the plant cells" in lines 4-5 makes the claim confusing. It is suggested that the phrase be deleted and "in the plant cells or in plants containing the plant cells" be inserted after "acetyltransferase" in line 5.

It is not clear in claim 60 what the practitioner of the invention must do to overexpress serine acetyl transferase in plants or plant cells already transformed with a nucleic acid encoding the enzyme. No step is drawn to inducing an inducible promoter, for example. It is suggested that the method be made one whose steps comprise transforming a plant cell, and optionally regenerating a plant from the plants cell, whereby the plant cell or the plant over expresses serine acetyltransferase and has an increase in production of cysteine, glutathione, methionine or sulfur-containing derivatives of methionine relative to a nontransformed plant or plant cell. Similarly, in claims 70-73, it is not clear what the practitioner of the invention must do to express the nucleotide sequence encoding serine acetyl transferase

12. Claims 72-73 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The methods are those of increasing the production of cysteine and other sulfur-containing compounds by plant cells and plants, and expressing the nucleotide sequence encoding serine acetyl transferase in plants. However, no plants are produced in the method steps. The omitted steps are those involved in production of plants.

Claim Rejections - 35 USC § 103

13. Claims 2-6, 9, 13, 17, 19-20, 24, 26, 60-63, 65 and 72-73 are rejected under 35 U.S.C. 103(a) as being unpatentable over Saito et al (1994, Plant Physiol. 106:887-895) in view of each of Noji et al (1998, J. Biol. Chem. 273:32739-32745) and Ruffet et al (1995, Eur. J. Biochem 227:500-509). The rejection is modified from the rejection set forth in the Office action mailed 17 June 2002, as applied to claims 2-6, 12-13, 17, 19-20, 23-26 and 60-71. Applicant's arguments filed 22 October 2002 have been fully considered but they are not persuasive. Applicant filed no arguments in the response of 17 December 2002.

The claims are drawn to a method of increasing the production of cysteine and other sulfur-containing compounds in a plant or plant cells by overexpressing an SATase in the cytoplasm, the mitochondria or the chloroplasts of the plant cells.

Saito et al disclose tobacco plants transformed with a construct encoding the spinach cytoplasmic cysteine synthase gene alone or fused to a Rubisco *ssu* transit peptide sequence (pg 889, right column, paragraph 3-5). The transit peptide-cysteine synthase constructs had an additional two amino acids between the transit peptide and the N-terminal portion of the cysteine synthase gene; these peptides would be the same as those from a mature N-terminal portion of a protein that is located in the plastids or would be the same as a second transit peptide. These constructs were properly transported to the chloroplast and correctly processed (pg 890, right column, paragraph 2). The resulting plants showed increased production of cysteine and resistance to sulfite (pg 891, left column, paragraph 2, to pg 892, left column paragraph 2, and Figure 6). Saito et al do not disclose plants transformed with a construct encoding SATase.

Noji et al teach genes encoding cytoplasmic, chloroplastic and mitochondrial SATase genes from *Arabidopsis*, their cysteine sensitivities, and the overexpression of the genes in *E.*

coli (pg 32742). The mitochondrial and chloroplastic forms would be fused to the native mitochondrial and chloroplastic transit peptides.

Ruffet et al teach a nucleic acid encoding a cytoplasmic SAT from Arabidopsis, wherein the SAT has a sequence of SEQ ID NO:2 (Figure 3, and pg 508, left column, paragraph 3).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the method of increasing the production of cysteine in a plant by overexpressing a cytoplasmic cysteine synthase in the cytoplasm and chloroplasts of a plant as taught by Saito et al, and to use a nucleic acid encoding another enzyme required for cysteine biosynthesis, SATase, as described in each of Noji et al and Ruffet et al. One of ordinary skill in the art would have been motivated to do so because of the role SATase has in regulation of cysteine biosynthesis Noji et al, pg 32744, left column, paragraph 4) and because Saito et al suggest expressing SATase in the plants for maximal cysteine formation (pg 893, left column, paragraph 1).

Applicant urges that Saito et al found no significant changes in cysteine and glutathione levels, as stated in paragraph 1, left column, pg 891 of that reference (response pg 14-16).

This is not found persuasive because Saito et al in Figure 6 and on pg 891, left column, paragraph 2, to pg 892, left column paragraph 2, show that transformed plants have much increased levels of cysteine over non-transformed plants.

Applicant urges that Saito et al does not suggest overexpressing SATase, but only suggest that plants transformed with a nucleic acid encoding cysteine synthase may require more SATase for maximal cysteine formation; Applicant urges that this sentence would require expressing both enzymes (response pg 16-17).

This is not found persuasive because of the open claim language in the claimed method. Expression of both enzymes is not excluded.

Applicant urges that Noji et al do not cure the deficiencies of Saito et al, alone or in combination. Applicant urges that combining Saito et al and Noji et al amounts to hindsight reasoning (response pg 17-19).

This is not found persuasive for the reasons indicated above. Noji et al teaches a nucleic acid encoding n SATase, required for the method suggested by Saito et al.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

14. Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over Saito et al (1994, Plant Physiol. 106:887-895) in view of each of Noji et al (1998, J. Biol. Chem. 273:32739-32745) and Ruffet et al (1995, Eur. J. Biochem 227:500-509) as applied to claims 2-6, 9, 13, 17, 19-20, 24, 26, 60-63, 65 and 72-73 above, and further in view of Svab et al (1993, Proc. Natl. Acad. Sci USA 90:913-917). The rejection is modified from the rejection set forth in the Office action mailed 17 June 2002. Applicant's arguments filed 22 October 2002 have been fully considered but they are not persuasive. Applicant filed no arguments in the response of 17 December 2002.

The claims are drawn to a method of increasing the production of cysteine and other sulfur-containing compounds in a plant or plant cells by overexpressing an SATase gene that is integrated into the chloroplasts of the plant or plant cells.

Saito et al in view of each of Noji et al and Ruffett et al disclose plants transformed with a construct encoding SATases fused to a Rubisco *ssu* chloroplast transit peptide sequence or the native chloroplast transit peptide. The resulting plants showed increased production of cysteine and resistance to sulfite. Saito et al in view of each of Noji et al and Ruffett et al do not disclose transformation of chloroplast with SATase gene-containing constructs.

Svab et al teach plastid transformation in tobacco (pg 914-915).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to increase the production of cysteine and other sulfur-containing compounds in a plant or plant cells by transformation with a construct encoding a cytosolic SATase fused to a chloroplast transit peptide sequence as taught by Saito et al in view of each of Noji et al and Ruffett et al, and to modify that transform the chloroplast as described in Svab et al. One of ordinary skill in the art would have been motivated to do so because the introduction of protein into the chloroplast by chloroplast transformation or by nuclear transformation with a construct that has a chloroplast transit peptide is an obvious design choice.

Applicant urges that Svab et al do not cure the deficiencies of Saito et al and Noji et al (response pg 19-20).

This is not found persuasive for the reason discussed above

15. Claims 23, 25 and 66-71 are rejected under 35 U.S.C. 103(a) as being unpatentable over (1994, Plant Physiol. 106:887-895) in view of each of Noji et al (1998, J. Biol. Chem. 273:32739-32745) and Ruffet et al (1995, Eur. J. Biochem 227:500-509) as applied to claims 2-

6, 9, 13, 17, 19-20, 24, 26, 60-63, 65 and 72-73 above, and further in view of LeBrun et al (1999, RE 36,449).

The claims are drawn to a method of increasing the production of cysteine and other sulfur-containing compounds in a plant or plant cells by overexpressing an SATase gene that is integrated into the chloroplasts of the plant or plant cells.

Saito et al in view of each of Noji et al and Ruffett et al disclose plants transformed with a construct encoding SATases fused to a Rubisco *ssu* chloroplast transit peptide sequence or their native transit peptides. The resulting plants showed increased production of cysteine and resistance to sulfite. Saito et al in view of each of Noji et al and Ruffett et al do not disclose plants transformed with a construct encoding an SATase fused to a optimized transit peptide.

LeBrun et al teach constructs encoding an optimized transit peptide comprises of the transit peptide of the small subunit of sunflower Rubisco, the N-terminal 22 amino acids of the maize Rubisco small subunit and the transit peptide of the maize Rubisco small subunit (claim 1).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to increase the production of cysteine and other sulfur-containing compounds in a plant or plant cells by transformation with a construct encoding a cytosolic SATase fused to a chloroplast transit peptide sequence as taught by Saito et al in view of each of Noji et al and Ruffett et al, and to modify that use the optimized transit peptide taught by LeBrun et al. One of ordinary skill in the art would have been motivated to do so because selection of chloroplast transit peptide is an obvious design choice.

16. Claim 64 is free of the prior art, given the failure of the prior art to teach or suggest a method of increasing the production of cysteine and other sulfur-containing compounds in a

plant or plant cells by transformation with a construct encoding a SATase fused to a transit peptide sequence of amino acids 1-63 of SEQ ID NO:6.

Conclusion

17. No claim is allowed.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (703) 308-5059. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Customer Service at (703) 308-0198.

Anne R. Kubelik, Ph.D.
April 17, 2003